
Is α -Keratin a Coiled Coil ?

ALL recent work¹⁻⁴ has confirmed that the structure of the synthetic polypeptide poly- γ -methyl-L-glutamate is based on the α -helix of Pauling and Corey¹. This structure gives a strong 1.5-A. reflexion on the meridian, and both MacArthur² and Perutz³ have shown that this reflexion also occurs in α -keratin. This suggests forcibly that the α -helix forms an important part of α -keratin.

There are certain difficulties in this idea. One of the main features of α -keratin is the strong reflexion at 5.15 Å. on, or very close to, the meridian. The normal α -helix gives strong reflexions on the 5.4-Å. layer line, but displaced from the meridian. The difference in spacing is not an insuperable objection, since the α -helix might be more tightly coiled; but it is difficult to see how one could obtain such a narrow meridional arc as is observed for α -keratin, even allowing for our ignorance of the details of the side-chain arrangement.

One way to bring the reflexion nearer to the meridian would be to tilt the α -helix. Since the α -keratin pattern is of wide occurrence, one would expect the tilt to be a constant feature of the structure. The most likely general solution is that the α -helix is bent into a super-helix, or coiled-coil. If the α -helix is twisted into a super-helix with a pitch angle of about 18° , its projection on to the axis would have a periodic variation in density at intervals of $5.4 \cos 18^\circ \approx 5.1$ Å., and so might explain the observed meridional reflexion which corresponds to this spacing. A pitch angle of 18° could be obtained, for example, from a super-helix of radius $10\frac{1}{2}$ Å. (the probable distance between helices) and axial spacing 198 Å. (the repeat of African porcupine quill)^{1,2}.

It is possible to make a rough estimate of the energy required to deform the α -helix by this amount by assuming that (1) the forces preventing small rotations about single bonds are small; (2) the hydrogen bond can be fairly easily deformed by small amounts in direction; (3) the main restoring force comes from the resistance of the hydrogen bonds to deformation in length.

Assuming a force constant for a hydrogen bond of, say, 3×10^4 dynes/cm. (see, for example, Davies¹⁰), the average energy per residue to deform the α -helix by the amount described above is about one-tenth of a kilo-calorie per residue, which is small. This energy increases roughly as the fourth power of the pitch angle, so that the α -helix can easily be bent through small angles, but resists large deformations.

So far, no reason has been given why the α -helix should be deformed. It seems probable that this is due to the difficulty of fitting together the side-chains of two adjacent α -helices.

I should like to suggest that there may be a general plan underlying the detailed packing of all the various side-chains found in proteins. If the side-chains of the α -helix are thought of schematically as knobs on the surface of a cylinder, then it is found that the pattern on this surface consists of knobs alternating with 'holes', that is, spaces into which the knobs from a neighbouring α -helix could fit. The position of these holes is roughly independent of the exact nature of the surrounding side-chains.

In poly- γ -methyl-L-glutamate, the side-chains are long and flexible and they can reach out towards the nearest hole without deforming the α -helix. In proteins, on the other hand, the side-chains are, on the average, smaller and less flexible, and neighbouring helices are nearer together ($10\frac{1}{2}$ Å. compared with 12 Å. for poly- γ -methyl-L-glutamate). It is therefore not unreasonable to simplify the undoubtedly complicated packing of side-chains into a set of standard rigid knobs fitting into standard holes.

It is impossible to pack such models of the α -helix closely side by side, since a good fit in one place produces a bad fit somewhere else, due to the non-integral nature of the helix. However, it can be shown that by deforming the helices into coiled-coils

the knobs can be made to interlock systematically. The energy for deforming the helices could come from the closer fitting together of the side-chains.

The objects of this communication are to stress that the α -helix can be deformed an appreciable amount if the deformation is systematic, to suggest that there may be a general plan underlying the packing together of side-chains, and to show that these two ideas lead to a coiled-coil which may explain some of the data¹¹ better than a straight α -helix.

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